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CHILDREN'S HOSPITAL

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Contents

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THYROTOXICOSIS IN A CHILD MANAGED WITH THIOURACIL*

Case Report No. 53

Dr. Frederic G. Burke 44–5431

D. H., a colored female, aged 10 years, was admitted to Children's Hospital on July 19, 1944 with the chief complaint of "puffiness of the neck." About 2 weeks before admission the child's mother had noticed a swelling of the anterior portion of the neck which had increased in size. The mother stated that she had been impressed by her daughter's eyes having a "staring" expression and appeared to bulge. This characteristic was most marked in the mornings, upon awakening. Concomitantly, the child developed a voracious appetite and despite this had lost weight. The exact amount of weight loss was not known. The child had become extremely "nervous" and "irritable." She had vomited on several occasions without apparent provocation. Dyspnea was noted upon exertion, and a doubtful history of palpitation of the heart was elicited. There had been no evidence of peripheral edema.

The child's past history was irrelevant. The maternal grandmother had been operated upon for "goiter" at the age of 45. The mother and father had no signs or symptoms of thyroid disease. A review of the systems was essentially normal. The patient had not yet begun to menstruate.

The patient was slender and well developed, in no apparent distress, and quite alert. There were no skin lesions or evidence of lymphadenopathy. The pulse rate was 120 per minute, the respiratory rate 16; the blood pressure was 150/60 in both arms. There was a mild degree of exophthalmos with a suggestive lid lag. The thyroid gland was asymmetrically enlarged, the left lobe being slightly smaller than the right. The right lobe measured approximately 6 by 3 cm. and the left lobe approximately 5 by 2 cm. The gland was firm and smooth. There were no nodules palpable. This mass moved with deglutition and was not tender. No bruit was heard. The lungs were apparently normal. The apical impulse was diffuse with a suggestion of a thrust. The rhythm was slightly irregular because of frequent extrasystoles. No murmurs were present. The abdomen was normal, and the extremities were normal, except for a fine tremor upon extension of the upper extremities. Quadriceps weakness was elicited by the stair-climbing test. Neurologic examination was essentially normal.

During the first 2 weeks in the hospital, while under observation, exophthalmos of a mild to moderate degree with infrequent blinking and stare

* This case was reported in the "Medical Annals of the District of Columbia" and is reported here by permission of Mr. T. Wiprud, Secretary.

were noted. The patient complained of choking sensations which were probably related to the cervical mass. Her skin was noted to be moist and warm, and a functional apical systolic murmur became manifest. Despite a good appetite, on a regular diet, the patient's weight decreased from 72 lbs., 4 ozs. to 71 lbs., 12 ozs. At the end of 8 days, upon continued bed rest, her weight picked up and at the end of 2 weeks she weighed 74 lbs., 4 ozs. Her pulse rate during the first week averaged 126 per minute, and her blood pressure at the end of 2 weeks in bed was 138/80. The basal metabolic rate 4 days after admission was plus 29 per cent and 2 days later 41 per cent. The blood cholesterol was 173 mgms. per 100 c.c. The sedimentation rate was 17 mm. per hour (Wintrobe and Landsberg method). Inorganic phosphorus of the blood was 5.3 mgms. and the calcium 10.4 mgms. per 100 c.c. Repeated urinalyses and blood counts were essentially normal. An x-ray film of the chest on the day after admission revealed the heart to be moderately enlarged to the left and right. One of the skull was reported as negative. An electrocardiogram taken on the eighteenth day after admission revealed only sinus tachycardia.

On August 3, 1944 the patient was placed on thiouracil (Deracil, Lederle Co.) and was given doses of 0.10 Gm. 3 times a day for 4 days. The dose was then reduced to 0.10 Gm. twice a day for 8 days and was then discontinued because of toxic symptoms. These were manifested by ringing in the ears, nausea and vomiting, rapid pulse, severe headache and slight fever (101°F). After 24 hours the drug was given again in doses of 0.10 Gm. once a day. No further toxic symptoms were noted. Her blood pressure fluctuated between 150/100 and 115/70 during the first 2 weeks while on this treatment but thereafter was normal. A basal metabolic rate determined on August 10, one week after thiouracil was started, was plus 34 per cent and repeated on August 16, two weeks later, was a minus 6 per cent. Blood cholesterol on August 8 was 193 mgms. per cent. An electrocardiogram 12 days after initiation of this treatment showed a normal record. At the end of 2 weeks her pulse rate remained consistently lower, despite activity around the ward. The thyroid gland was thought to be smaller, the staring expression and lid lag disappeared, and the exophthalmos became less prominent. She felt well, and at the time of discharge on September 8, 1944, 50 days after admission, she weighed 77 lbs. Subsequent basal metabolic rates taken at weekly intervals were minus 6 and minus 4 per cent.

The patient was seen in the outpatient department 3 weeks after discharge, having been sent home on a maintenance dose of 0.10 Gm. a day of thiouracil. The basal metabolic rate at this time was plus 5 per cent.

Subsequent examinations made at weekly intervals revealed the patient

to continue in good health; she had gained 20 pounds over a period of 2 and a half months, the length of time she had been on thiouracil. The drug was discontinued for 1 week, 5 weeks after discharge from the hospital because of leukopenia (3,900), with, however, a normal differential, hemoglobin and red blood cell count. Seven days afterwards it was begun again at the previous dose, the white count rising to 10,000. Observation will continue at weekly intervals and she will receive brewer's yeast and liver extract (as recommended by Williams and Clute[1]).

Discussion

Toxic goiter is a relatively uncommon occurrence in children. At the Crile Clinic[2], in Cleveland, there were but 42 cases in children under 14 years of age in a series of 13,200 cases of hyperthyroidism. The Mayo Clinic[3] reported 157 cases of exophthalmic goiter in children 14 years or less, among 15,505 cases seen at that institution, an incidence of slightly more than 1 per cent. This latter series of cases, reported by Roger L. J. Kennedy, comprises the largest and most reliable set of statistics of this disease in children. One hundred thirty-six of the cases reported by Kennedy were treated surgically after a preoperative course with Lugol's solution, most of whom had been given a trial on a medical regimen. In childhood, obviously, a successful medical management of this disease would have tremendous advantage because of the important rôle the thyroid gland plays in development. Most workers agree that, in spite of the best medical care and treatment, surgery is found necessary in the vast majority of cases.

Kerley[4] gave medical measures a trial of at least 1 year before advising surgical interference. In his report of 104 cases of hyperthyroidism in children, the majority eventually were treated surgically.

Reilly[5] reported operative treatment in 55 per cent of the 62 patients he treated over a period of 10 years after failure of a medical regimen to control the toxicity of the disease.

Despite the importance of the thyroid hormone in the growth and development of the child, thyroidectomy has been necessary in the successful management of toxic goiter in most of these patients. A low percentage may be successfully treated by bed rest, the judicious use of iodine, psychotherapeutic and other medical measures, but nearly all reports agree that removal of the gland is eventually necessary in the majority of cases.

Not too much information is available regarding the detailed follow-up of children who have had a thyroidectomy. A recurrence rate of approximately 8 per cent is a generally accepted figure, and hypothyroidism and hypoparathyroidism are not rare complications. Kennedy reported a

reduction in the surgical mortality rate of toxic goiter from 9 to 2.5 per cent due to the use of iodine. The operative mortality rate throughout the country, however, is probably higher.

The recent literature contains many reports concerning the effectiveness of thiouracil in the treatment of hyperthyroidism in adults. This drug has been used in several thousand cases up to the present time in this country, and there is uniform agreement upon its beneficial influence in thyrotoxicosis. Recent investigations have centered more upon the toxic effects of this drug, especially as it affects the hemopoietic system. There have been at least 7 known deaths due to agranulocytosis and leukopenia attributed to this method of treatment. However, in well controlled series, such as reported by Williams and Bissell[6], and others,[1, 7] no serious toxic results have been noted. It appears, therefore, that an extremely valuable addition has been made to the medical armamentarium for the treatment of hyperthyroidism. It is not possible to state whether patients may be controlled indefinitely with this drug, but it would seem an extremely advantageous procedure to be followed in children with this disease in consideration of the relatively more important rôle of the thyroid gland to these subjects.

The case reported here indicates, at least, the value of thiouracil in bringing about a remission of the toxic symptoms of hyperthyroidism for an indefinite period of time. While surgical removal of the gland might become an eventuality, it is believed that the longer this can be delayed the more this patient will benefit.

Interval note. Thiouracil therapy was maintained for one year after which time it was stopped. At the end of a year the child on physical examination and laboratory check-up was normal in every respect. Following a recent examination one year after the cessation of treatment this child has remained asymptomatic and her physical examination is normal.

REFERENCES

(1) Williams, R. H., and Clute, H. M.: Thiouracil in treatment of thyrotoxicosis; report of 7 cases. New England Journal of Med., 1944, **230**, 657.

(2) Crile, G., Jr.: Hyperthyroidism in extremes of life. Cleveland Clin. Quart., 1938, **5**, 117.

(3) Kennedy, cited by Brennemann, J., ed.: Practice of Pediatrics, vol. 1, chap. 38. Hagerstown, Md.: Prior, 1937.

(4) Kerley, C. G.: Hyperthyroidism in children. Arch. Pediat., 1941, **58**, 92.

(5) Reilly, W. A.: Thyrotoxicosis. Am. J. Dis. Child., 1940, **60**, 79.

(6) Williams, R. H., and Bissell, G. W.: Thiouracil in treatment of thyrotoxicosis. New England J. Med., 1943, **229**, 97.

(7) Watson, E. M., and Wilcox, L. B.: Thiouracil in treatment of thyrotoxicosis. Canad. M. A. J., 1944, **51**, 29.

*SPECIAL REPORT**

ALLERGY IN PEDIATRICS

Dr. Dorothy Jaeger Lee

A well known allergist of our day justly says, "Without some knowledge and application of the principles of allergy, modern pediatrics cannot be practiced." The pediatrician sees many instances of allergy and is often fortunate enough to detect them at their very beginning. Asthma, stuffy irritable noses, infantile eczema, spasmodic coughs, unexplained abdominal pain and vomiting, and colic are common complaints. The pediatrician in his routine check-ups is apt to catch them in their beginnings and, because of this, is often able to check these atopic conditions before a more complicated diet and environment is given the young child. This early detection can help to prevent trouble for these young patients in their future years.

A positive family history is obtainable in about 70 percent of the cases. In these cases, children seem to inherit the capacity to become sensitized. The particular allergens to which the child becomes sensitized depends upon his diet and environment. At first, usually the allergens are foods, in time inhalants may be added to the list. Eczema is most common within the first six months of life; later asthma appears and often, at about puberty, hay fever. In other words, there is a definite succession of symptoms, all a part of the same process.

In a way of a brief review, allergy is the abnormal reaction of tissues to physical or chemical stimuli. The mechanism of this reaction is still not clearly understood but the two most popular explanations are the *humoral* and *cellular* theories. In the *humoral* theory it is supposed that the reaction between the antigen and antibody takes place in the circulation, giving rise to an anaphylotoxin which acts on the shock organ and produces the abnormal response. The advocates of the *cellular* theory believe that the antigen-antibody reaction takes place directly in the tissue cells, resulting in the development of the "H" substance which is either identical with or resembles histamine, and this "H" substance causes the allergic response.

Allergic responses or hypersensitiveness may be classified as follows:

1. *Anaphylaxis.* This type of hypersensitiveness is confined to the lower animals. It is produced by a sensitizing dose of antigen and a subsequent shocking dose of the same antigen. No hereditary factor is present, and successful temporary desensitization may be accomplished. Anaphylaxis

* This report was made to the weekly Staff Conference as a discussion to several cases of Infantile Eczema that were presented.

differs from the so-called "anaphylactoid reaction" or immediate serum reaction that may follow the administration of an animal serum. In the case of the latter positive skin tests show the presence of sensitivity to the animal serum. This sensitivity to horse serum arises from one of two possible sources, previous injections of the serum or a naturally acquired sensitivity to horse epithelium. Horse dander contains two antigens, the dander antigen and a small amount of the serum antigen. Fever, circulatory collapse, generalized urticaria, rhinitis, tightness in chest and asthmatic wheezing are the distressing symptoms that occur immediately or within a few hours after the administration of the serum. The outcome may be fatal. It is important that skin tests be performed before the administration of animal sera.

Immediate serum reactions, unlike serum sickness, are due to sensitiveness to serum prior to the injection of the reacting dose and unlike serum sickness the likelihood of its occurrence can be forecast by tests preceding the administration of serum.

2. *Atopy.* Atopy is a group of clinical manifestations characterized by localized tissue edema and/or increased activity of smooth muscle. The shock organ determines the response; for example, if it is the skin, the result is eczema or hives, or, if it is the bronchi, it is asthma, etc. This group of conditions is of chief concern and interest to the pediatrician. In it are included hay fever, asthma, alimentary allergy, and skin allergy. The following characteristics are present in atopy:

1. Skin tests are positive. This is shown by immediate whealing reaction upon cutaneous or intracutaneous application of the allergen. This may also be demonstrated in passive transfer by injecting patient's blood serum intradermally in the skin sites of a donor and testing these areas.

2. The allergen or antigen is usually a protein molecule or is attached to a protein molecule.

3. An hereditary nature is exhibited. In other words, the tendency to become sensitized and manifest symptoms seems to be an inherited quality in most instances.

4. Desensitization may be accomplished by numerous injections of the allergens over a long period of time. This is sometimes a difficult procedure.

3. *Drug Allergy.* Probably drug allergy should be classified under atopy, but this differs from atopy in several respects. The responses are usually produced by simple non-protein compounds such as aspirin, barbiturates, coal tar products, etc. Skin tests are negative to the compound causing the response.

4. *Bacterial Allergy.* The best classical example of bacterial allergy is the tuberculin test. Heredity is not a factor. Infection is necessary. A delayed response occurs to intradermal testing, consisting of a papular lesion

with edema and hyperemia twenty-four to forty-eight hours after testing. Studies in the field of bacterial allergy have opened up a fascinating new approach with vast possibilities to many diseases such as rheumatic fever, nephritis, arteriosclerosis, etc.

5. *Contact Types.* In this type of allergy the reaction is in the upper layers of the skin and it is brought about by direct contact of the allergen on the skin surface. The hereditary factor is not definitely present but there seems to be present a constitutional predisposition. The antigen is not a protein but usually a resin, lipoid or chemical substance, such as a heavy metal. Positive patch tests are present, that is, after the substance is left in contact with the skin 24 to 48 hours redness, vesiculation and itching result. Desensitization may be accomplished when the antigen is a lipoid, such as in the case of poison ivy.

6. *Serum Sickness.* The symptoms of serum sickness, urticaria, fever and joint pains, that occur several days after the primary injection of animal sera, are familiar to the pediatrician. In this type of allergy there is no hereditary factor, skin tests prior to injection of the serum are negative, and there must be an injection of a protein in the form of a serum.

7. *Physical Allergy.* The abnormal response to physical agents such as heat, cold and light is difficult to explain and can produce the same symptoms as those described under atopy. Usually atopy is also present. It is impossible to demonstrate passive transfer of this type of hypersensitiveness.

Besides the primary sensitizing factors that cause allergic diseases, many secondary causes have been demonstrated. Quite often these secondary causes may precipitate an attack or be a predisposing influence for the initiation of a specific hypersensitiveness. In other words, they disturb the patient's "allergic balance." These secondary causes are:

1. Mechanical—Dust is the best example even when it does not necessarily contain the specific antigen. Chalk dust in schoolrooms often aggravates an allergic rhinitis. A ride along a dusty road may precipitate an asthmatic attack. Irritation from clothing may intensify eczema. The mechanical factors produce their effect via mechanical irritation.

2. Chemical—Strong odors as from paint, perfumes and gasoline will aggravate allergic rhinitis or asthma.

3. Thermal—Sudden temperature changes, as going from a hot house to cold air, or hot baths, may upset a patient's "allergic balance."

4. Infection—Upper respiratory infections distrub the patient's allergic equilibrium and tend to maintain the allergic state. Likewise, allergic changes in mucous membranes lowers the resistance of these tissues to infection, as in sinusitis, so that the process represents a "vicious circle." Allergic symptoms may disappear during or after high fever.

5. Nervous and Psychogenic—Excitement, fatigue, fear and nervous

fatigue may precipitate an attack of asthma, hay fever or hives. For example, one of my patients broke her arm and was told she would have an anesthetic the next morning to set the bones. She recalled an unpleasant previous anesthetic induction and that night developed a severe attack of asthma.

6. Endocrine—The exact relationship of the endocrines to allergic diseases is not clear but it is possible that ovarian hormones have some connection, since frequently symptoms vary at puberty, menstruation, pregnancy and menopause.

7. Physical Exertion—Running, lifting and other forms of physical exertion aggravate asthma and allergic rhinitis. In some cases it is wise to keep patients from gymnasium classes since active exercise may cause coughing and wheezing.

8. Constipation and Indigestion—Gastro-intestinal disturbances upset the "allergic balance" and therefore aid in the production of atopic symptoms.

The discussion of diagnosis and treatment will be limited to atopy since these are the important clinical manifestations of hypersensitiveness.

A very detailed history must be obtained. Not only will it help to establish the correct diagnosis but it is of great aid in the management of the patient. The age of onset and conditions under which the patient was living at that time should be thoroughly investigated. Was the house in town, near a stable or mill? What furnishings were in the room? Did they have any pets?

The frequency and length of attacks with seasonal variations may give a clue. When the symptoms are worse in spring maybe grass or tree pollen is the cause. In August ragweed pollen may be the offender. How does the patient obtain relief if any? Does shutting the windows help? Quite often the patient can sense the antigen to which he is sensitive. For instance, face powder may make him sneeze or cough. His nose may become stuffy or he may start to wheeze when he goes to bed with a feather pillow. Egg or other foods may cause his mouth to itch. The presence of secondary causes, mechanical, chemical, thermal, physical, psychogenic and infectious should also be determined.

Certain laboratory tests may be helpful in determining whether the complaint is allergic or not. Often, eosinophilia is present in the peripheral blood. The mucous discharge from the nose is usually packed with eosinophiles in allergic rhinitis.

Skin tests are preformed for the most common inhalants, pollens, molds, and foods. Scratch tests with dried extracts and pollens may be used, or intradermal tests. Both have their advantages and disadvantages. Some workers feel that intradermal tests produce more false positives than scratch

tests, but with good technique, non-irritating solutions and using diluting fluid as a control test these can usually be overcome. Intradermal tests are used exclusively in the Allergy Clinic at Children's Hospital. These are performed with short bevelled 26 gauge, Schick Test needles and Cook allergy syringes. Just enough testing solutions (probably 1/100 cc.) to form a minute wheal is injected intradermally. In children we use a series of six to eight tests at a time, spacing the tests about two inches apart and endeavoring to inject the same amounts of solution in each individual test site so that results can be properly evaluated. Tests are read about 15 to 20 minutes after injection and classified as negative, slight, moderate, and marked. Positive skin tests are usually interpreted as the cause of the allergic complaint. But this is not always true. Positive skin tests may be present because of an associated clinical allergy, a sub-clinical allergy, a past clinical allergy or future or potential allergy. Also, positive tests may result because of a genetic relationship of allergens, urticariogenic substances (such as morphine and histamine), irritating substances in extracts (glycerin) or dermatographism. Therefore the cause of the allergic complaint should not be determined by skin tests alone. A thorough history and properly evaluated skin tests should be combined in the diagnosis. These should be confirmed by clinical tests when possible. Clinical tests consist of removing the allergen from the diet and environment with subsequent improvement of the patient. Unfortunately, usually more than one allergen is responsible, so that the procedure is usually not very simple.

The question of the value of food tests is debatable. The extracts used for testing are made from the foods themselves. It stands to reason that it is not usually the food in its ingested form that acts as the allergen when is it absorbed from the gastro-intestinal tract. By the time the food is ready to be absorbed it has been changed into an entirely different chemical compound by the digestive enzymes. Some food extracts, too, contain irritating substances. The late Dr. Vaughn of Richmond found that 60 to 90 minutes after the ingestion of food to which the patient is hypersensitive a drop of 1000 or more occurred in the white cells of the peripheral circulation. And so he developed what is now known as Vaughn's leukopenic index. Because of the large varieties of food this test has limited possibilities unless a group of foods is used at a time.

The treatment of atopic manifestations is twofold, specific and general. Prophylactic treatment too should probably be added for the pregnant woman who knows that there is a history of allergy in either family or parent. In this way she may prevent at least early allergic manifestations in her child. This is done by avoiding excess of any one food and eating small amounts of all foods unless she herself is allergic to certain foods.

Specific treatment consists in removing the antigens, if possible, from the diet and environment, and if practical desensitization with the offending antigen. Dust is the most common offender. Allergen-proof covers should be placed on the mattresses and pillows. Kapok is just as bad if not worse than feathers since after several years even the best of Kapok powders to dust. It is best that the patient have a room of his own. Furniture should be simple and easily cleaned. Comforts and soft toys harbor dust and are therefore to be avoided. The rugs and curtains, if any, should be washed frequently. Bookcases and toy cupboards without doors are banned. If the room is heated by hot air, filters should be placed over the registers.

If important foods, for example milk or wheat, must be eliminated from the diet substitutes must be added. Soy bean preparations, goats milk or an enzymic digest of milk may replace milk. Rice, corn meal, oats, barley, etc. can be used in place of wheat. It is important if there is any question of deficiency that the essential minerals and vitamins be added to the diet.

Desensitization is a slow and tedious process. More harm can be done by overtreatment than by no treatment at all. Small amounts of diluted extract are injected sub- or intracutaneously at first and then gradually increased in amount depending upon the patient's symptoms and reaction at the site of injection. It is best to have the patient wait twenty to thirty minutes after one injection to determine the reaction at the site of injection and also to make sure he does not develop a systemic reaction. Oral desensitization is carried out for common foods such as wheat, milk, egg, orange, tomato and chocolate.

Desensitization to all of the offending antigens is not always practical. For example dogs and cats can easily be eliminated from the environment. If orris causes symptoms a face powder that does not contain orris should be used.

Secondary factors such as mechanical and chemical irritants that upset the patient's "allergic equilibrium" should be removed, if possible, or controlled. The patient must be kept in the best physical condition. If the diet has been limited supplements are added as well as a more than adequate intake of vitamins. Rest is very important. Exposure, especially to upper respiratory infections, should be avoided.

Of course, symptomatic treatment depends upon the shock organ affected. Ephedrine by mouth or epinephrine intramuscularly, the dosage depending upon the age of the patient, temporarily relieves most of the symptoms except those of eczema and gastro-intestinal allergy. Epinephrine in oil has a more prolonged action of 6 to 8 hours. Aminophyllin may be given in cases of asthma resistant to epinephrine but must be used cautiously. In our hospital several times when given supposedly intramuscularly it has produced sterile abscesses or when given too rapidly and

in too large amounts intravenously it has produced profound shock, necessitating intravenous fluids and cardiorespiratory stimulants.

Expectorants such as iodides in the form of syrup of hydriodic acid should be given to thin the bronchial secretions in asthma. Steam will give great relief in acute attack. Antispasmodics sometimes aid in granting rest to the patient but depressants, especially morphine and codeine, should be avoided.

In cases of allergic rhinitis it is often necessary to use nose drops to shrink the boggy mucous membranes. These drops must be mild and isotonic, so as not to cause more congestion or impair ciliary action.

Infants and children with eczema should avoid soap and water. Mineral oil baths are usually used. Secondary infection is treated with ammoniated mercury ointment or sulfonamide or penicillin ointment. Restraints to avoid excessive irritation or subsequent infection may be necessary in the small child. Coal tar products in the form of ointments allay itching. Ointments containing salicylic acid thin the thickened areas.

It is obvious that the ideal treatment of allergic diseases with subsequent cure has not yet been found. Much work has been done along the lines of desensitization with histamine and histamine-like substances, but this is still really in the experimental form. Large doses of Vitamin C in vogue several years ago have not been satisfactory.

REFERENCES

GLASER, JEROME: Pediatric Allergy. Annals of Allergy, Sept. & Oct., 1944.
PRATT, LT. COL. HENRY W.: Proceedings of Royal Society of Medicine, May, 1944.

STUDY OF CHILD HEALTH SERVICES

The Study of Child Health Services, sponsored by the American Academy of Pediatrics, is well launched in the District under the direction of Dr. Edgar P. Copeland, Chairman of the Academy for the District of Columbia

The purpose and scope of this physician's study of facilities now available for the treatment of children have been presented to the medical profession through various mediums. All physicians are doubtless familiar with the ultimate objective of the Study "To make available to all mothers and children in the U. S. A. all essential preventive, diagnostic and curative medical services of high quality, which, used in cooperation with other services for children, will make this country an ideal place for children to grow into responsible citizens."

To attain the three-fold purpose of the Study the active cooperation of every practicing physician is necessary. It is the physician's privilege to participate in collecting data to:

1. Determine the distribution among practicing physicians of the load of the medical care of the youth of the nation.

2. Evaluate the status of existing and non existing health facilities as found by practicing physicians in the medical care of their young patients.

3. Furnish accurate factual data on which future planning for adequate child care can be based.

With such material available a measure of the health facilities of the nation and of the component States will become known to the medical profession. The information will serve as an index on which the differential health needs for the betterment of health facilities in each community can be determined.

All practicing physicians in the District of Columbia have been asked to do their part in this Study by giving conscientiously their share of pertinent information. It is fully recognized that all doctors are exceptionally busy at this time, and for that reason plans for obtaining the necessary information have been simplified as much as possible.

Two questionnaires have been distributed to physicians:

The first, under the title Schedule III-B, has been sent to all pediatricians and to those physicians primarily interested in practice of pediatrics. These schedules are designed to cover detailed information concerning work done over a period of one month. Instructions for completion accompany these schedules and the fact is emphasized that information covers office, home and hospital visits to private patients only.

The second schedule, under title III-A, has been sent to all physicians in

private practice. This schedule calls for a one-day record of practice. The questionnaire is self explanatory with emphasis placed on specific *day* of the week rather than definite *date*.

Complete and accurate information is essential in determining the extent and quality of existing facilities for treatment of children. In furnishing the information requested on these questionnaires the physician will be contributing an individual answer to two fundamental questions, based on personal medical experience and knowledge of the status of youth health facilities in the community in which he practices; To what degree does he, as a physician, carry the load of the medical care of young patients in this community and have the health facilities in this community met his medical requirements in carrying out the medical care he wishes to give his young patients?

The American Academy of Pediatrics, with the assistance of the U. S. Public Health Service and the U. A. Children's Bureau have undertaken this tremendous task. The success of the Study, however, is wholly dependent upon the full and prompt cooperation of every practicing physician. With such assistance the Study of Child Health Services in the District of Columbia should reach a successful conclusion within a relatively short time.

This Study is a challenge to physicians to investigate their own affairs, to discover for themselves the needs within their own communities and to evaluate existing facilities. Unless physicians complete this task, others less well qualified will—as indicated by various bills now before Congress.

FOREIGN BODY VAGINITIS

Case Report No. 54

Dr. Clifford Tichenor and Dr. Frances Ayers J. W.-40-9346

J. W., a colored female, age 8, was brought to the hospital because of a bloody vaginal discharge. The patient had had a creamy vaginal discharge recurrently for a period of a year, and had seen two doctors who had cleared the discharge temporarily, but it recurred each time. She began to have a profuse bloody discharge with clots about one week prior to admission and came to The Children's Hospital Gynecological clinic, where smear and culture were taken and the patient given sulfadiazine. Gram negative diplococci having the morphology of gonococci were found by the laboratory on one occasion. There was no response to sulfonamides however, and she was admitted March 5, 1946 because of persistent bloody discharge.

The past history was non-contributory except for having had the common childhood illnesses and pneumonia at the age of 2. Family history was negative for any blood dyscrasias, venereal disease, tuberculosis or diabetes.

Physical examination revealed a well developed, well nourished colored female of about the stated age, not appearing acutely ill, in whom the only positive finding was a bloody vaginal discharge. It was thought that this discharge had the appearance of gonococcus vaginitis and treatment was instituted in the form of oral penicillin, 50,000 units every 4 hours for 6 doses, or a total of 300,000 units.

The vaginal smear, however, was negative for gonococci according to the laboratory report. However, smears are considered to be not always a reliable criterion, and the assumption was continued that this was a specific vaginitis, to be treated as such until proven otherwise.

Repeated vaginal smears were negative for gonococcus and vaginal culture showed no growth of any gram negative diplococci. Stool examination showed no ova or parasites. Kahn and Mazzine were negative.

One week after admission vaginal smear showed gram negative organisms to be present and vaginal culture showed non-hemolytic staphylococcus and E. coli. The urine was turbid, acid, specific gravity 1.014, and microscopically showed very numerous white blood cells in clumps; albumin was negative. On no occasion was trichomonas vaginalis found. It was decided to begin sulfadiazine one week after admission, since there was no clinical response to penicillin.

On the 14th day of her admission, an x-ray of the pelvis was taken in the A. P. view which revealed a safety pin in the region of the vagina.

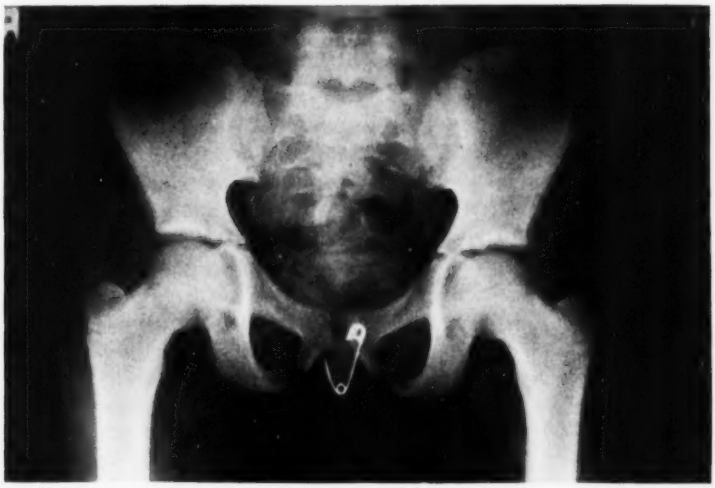


FIG. 1. J. W. NOTE SAFETY PIN IN VAGINA

On the 16th day a small brass safety pin in three sections was recovered from the vagina. One end of the pin was sticking in the cervix. The hymenal ring was much traumatized, one piece lying free in the vaginal canal. After removal of the foreign body the canal was flushed with a mild antiseptic and an iodoform pack inserted temporarily. Her recovery was prompt and uneventful.

DIFFERENTIAL DIAGNOSIS

Dr. Frances Ayers: The commonest cause of vaginal discharge before puberty is infections, either gonorrheal or non-specific. It is well to remember that non-specific vaginitis is frequent, probably more so than that of gonorrheal origin. Another point of importance to be borne in mind is the similarity of the gonococcus to other organisms, especially micrococcus catarrhalis, pseudogonococcus and meningococcus. It is only by careful physical examination and studies of smears and cultures that the diagnosis of gonorrhea can be made. Among the organisms causing a nonspecific vaginitis are the pseudodiphtheria bacilli, pseudogonococcus, the staphylococci, streptococci, gram negative cocci and bacilli of the Bacterium coli group and micrococcus catarrhalis.

There are a number of other diseases which may result in genital infections and vaginal discharges. Diphtheria may begin as a vulvovaginitis

or be transplanted from a throat infection. Trichomonas may cause a vaginitis and discharge. Dysenteric infection of the vagina has been reported as has pinworm invasion from the rectum. Neoplasms of the vagina and uterus although rare must always be considered in the differential diagnosis especially since they are so often malignant.

Traumatic vaginitis must always be ruled out, especially when the vaginal discharge is associated with bleeding. Safety pins, hairpins, and crayons have all been found.

THROMBOCYTOPENIC PURPURA

Case Report No. 55

Dr. Ralph Stiller H. S.—42-9786

This is the case of H. S., a 7 year old colored male, who was admitted to Children's Hospital on March 26, 1946 with the chief complaint of "purple spots on his chest and legs" appearing the morning of the day of admission.

The present illness goes back 4 days at which time the child had a minor nose bleed, lasting one hour. He had also been bleeding from the gums around a decayed tooth for the preceding 2–3 days. The morning of the day of admission purple spots were noted on his chest and legs. No history could be elicited of hematemesis, melena, or hemoptysis. There was no history of excessive bleeding or bruising in the past. Review of systems were entirely negative.

The child had a normal birth and development and the past history included an attack of infantile eczema, tonsillitis two to three times, and measles. There were no other childhood diseases. There was no familial incidence of excessive bleeding, jaundice or anemia. One paternal aunt had tuberculosis but the child was at no time in contact with her.

Physical examination on admission revealed a well developed, well nourished 7 year old colored male lying quietly in bed in no distress, with petechiae of the sclera, trunk and extremities. Significant findings in addition to these were: a decayed lower left molar around which the gum was bleeding moderately; tonsils were hypertrophied and hemorrhagic; a small amount of blood was present in the anterior nares; there was no significant lymph node enlargement; liver and spleen were not palpable; the Rumpel-Leede test for capillary fragility was positive.

Laboratory work-up revealed a hemoglobin of 10 grams, 3,200,000 erythrocytes, 8,100 white-cell count with 51% neutrophiles. Platelet count was 5000. Coagulation and bleeding times were 3 minutes and 1 minute respectively. Prothrombin time was 98% of normalcy. Urine was negative.

Sternal biopsy revealed an essentially normal marrow with the exception of an increase in the number of eosinophiles and an apparent absence of thrombocytes and megakaryocytes.

With these facts known, the diagnosis of idiopathic thrombocytopenic purpura was considered. It was suggested by Dr. Rice that an allergic factor might be present on the basis of the eczema in infancy and the predominating eosinophilia in the marrow biopsy.

The hospital course consisted of almost persistent bleeding from the nose which was counteracted by frequent transfusions, a total of 2000 cc. of

blood having been given from the day of admission until the day of operation, April 21, 1946. Despite this the blood count varied from 2,100,000 to 3,500,000 with hemoglobin determinations of from 6.5 to 10 grams. Platelets were consistently absent. The temperature curve fluctuated from 98.6° to 100° throughout his preoperative course. From the 3rd of April until the 10th moccasin venom was given in gradually increasing doses from 0.4 cc. to 1.00 cc. but produced no hemostatic effect.

On the 20th of April after having gone a week with only a few transient bleeding episodes, a splenectomy was done. There has been no bleeding since then, the postoperative course has been uneventful and daily platelet counts have shown the following result:

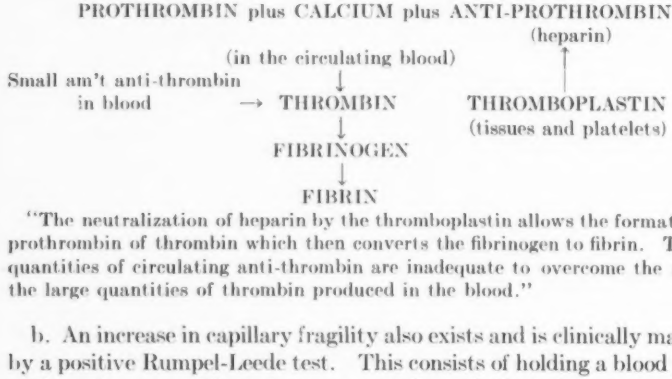
April 21—90,000; April 22—700,000; April 24—275,000; April 26—1,000,000; April 27—600,000.

From a postoperative count of 2,400,000 red blood cells, the blood picture now shows 3,800,000. There have been no blood transfusions postoperatively.

DISCUSSION

Essentially thrombocytopenic purpura is a bleeding disease occurring most commonly between the ages of two and ten, and more common in females than in males though not strikingly so. The etiology is unknown although some few cases have suggested an hereditary element. This is far from the usual case.

The basic defects are two-fold: a. Primarily there is a lack of circulating thrombocytes which results in a failure of clot retraction. This suggests a quantitative defect in fibrin possibly due to insufficient thrombin formation. If we recall the Howell theory of blood coagulation[1]—



"The neutralization of heparin by the thromboplastin allows the formation from prothrombin of thrombin which then converts the fibrinogen to fibrin. The small quantities of circulating anti-thrombin are inadequate to overcome the action of the large quantities of thrombin produced in the blood."

b. An increase in capillary fragility also exists and is clinically manifested by a positive Rumpel-Leede test. This consists of holding a blood pressure cuff on the arm midway between systolic and diastolic pressures for ten

minutes. A shower of petechiae distal to the cuff is considered a positive finding.

In addition to the platelet count and Rumpel-Leede test two other laboratory tests are the coagulation time which is usually normal and the bleeding time which is usually prolonged.

Cooley divides the clinical types into four: 1. Chronic recurrent, in which there are periodic bleeding episodes with intervening good health and platelet counts normal at times, depressed or absent at others; 2. Mild forms in which petechiae are present most of the time with no serious bleeding episodes; 3. Fulminating attacks that cause death soon after the onset of the first attack; 4. Those who have one attack, recover and are not seen again. One can wonder whether they are cases of essential thrombocytopenic purpura, as they could well be transient episodes of a secondary thrombocytopenia.

It must be remembered that this differential is extremely artificial; that a mild form may suddenly exacerbate in a fulminating manner and that one is never justified in lapsing into a false sense of security. The artificiality of this breakdown is apparent when one tries to classify such a case as is presented here (H. S.). One is inclined to consider the patient as belonging to the chronic recurrent group but this is an assumption as splenectomy was done prior to a pronounced remission. He might well have been a fulminating type saved by splenectomy.

Differential Diagnosis

To recapitulate, the salient points in making the diagnosis of essential thrombocytopenia are a failure of clot retraction, low (under 60,000) or absent platelets and a positive Rumpel-Leede test. These together with bleeding, or a petechial eruption and anemia, are almost pathognomonic. The chief differential is secondary thrombocytopenia. Marked leucopenia of leucocytosis is suspicious of this as is the presence of abnormal or immature cells. Aleukemic leukemia and aplastic anemia must also be considered in the differential diagnosis. The former may be impossible to differentiate without a marrow biopsy and this should always be done before sending the patient to surgery. A normal bone marrow or one showing a diminution of megakaryocytes is consistent with primary thrombocytopenia. To quote Cooley's article in Brennemann[2], "Infection plays a large part in the production of thrombocytopenia. When the thrombocytopenia appears in the course of an infection, it often seems to be of the nature of hypoplasia or aplasia of the megakaryocytes which may clear up entirely with the passing of the infection. On the other hand, and this is more common, infection may be followed by thrombopenia due to platelet destruction, from which there may be complete recovery, or the condition

may recur with subsequent infections; or the infection may bring to light the constitutional peculiarity which is probably at the base of essential thrombopenia. It is not always possible to distinguish between these conditions at first sight. The real difficulty lies in deciding whether a first attack of thrombocytopenia or a type that recurs with repeated infections is really an essential form, or only symptomatic, and there is no way of settling this question except by observation, with diligence eliminating foci."

Treatment is directed primarily to checking bleeding. Frequent small transfusions are best. Fresh blood is desirable as platelets do not last long in bank blood. These are given to tide the patient over the acute phase of the attack and to prepare him for splenectomy. Snake venom and antivenon have been tried in an effort to stop the bleeding with questionable success. The rationale of their use is not too clear.

Splenectomy has been found to be of definite benefit in this disease. Several theories have been advanced as to the connection that the spleen has with thrombocytopenia in an attempt to explain the beneficent effects of splenectomy. Kaznelson's belief that the platelets are destroyed by the spleen is the one most widely held. Splenectomy is a serious operation and should be done at a favorable stage in the disease although it may be a court of last resort in an intractably bleeding case. Blood should be given before, during and following the operation. Platelets rise to a peak high above normal a few days post-operatively and then subside to normal in most cases. In some cases the platelet count stays low but there is no bleeding. Occasionally relapses have occurred and proven due to the presence of an accessory spleen. It seems well established that if all splenic tissue is removed in a case of primary thrombocytopenia the bleeding stops. Failure of cure in the presence of total splenic extirpation is presumptive evidence against the diagnosis of the primary type of thrombocytopenia. It would seem that even in the mild cases with little or no bleeding splenectomy is advisable as one never knows when such a case may present a fulminating picture.

REFERENCES

(1) Best and Taylor: Physiological Basis of Medical Practice, pp. 142–144.
(2) Brennemann: Practice of Pediatrics, Vol. 3, Chap. 17, pp. 6–11; Prior & Co., Hagerstown, Md., 1944.
(3) Holt and McIntosh: Diseases of Infancy and Childhood, pp. 568–572; Appleton-Century, N. Y., 1944.

CLINICO-PATHOLOGICAL CONFERENCE

Directed by: Dr. E. Clarence Rice

Assisted by: Dr. Robert B. Sullivan

Dr. Robert B. Sullivan

A nine year old colored boy entered the hospital on April 12, 1945, because of epigastric pain of two days' duration. The pain was rather sudden in onset, was constant, and prevented the patient from lying flat in bed. He lacked appetite but there had been no nausea, vomiting or diarrhea. For several days before the onset of the illness he had fallen and hurt his right knee which continued to be mildly painful.

He had had frequent colds but no other illnesses. The parents and four siblings were well and the family history was non-contributory.

The boy was well developed and well nourished but was acutely ill. He appeared toxic, feverish, listless and slightly acidotic. His temperature was 103.2 and his pulse 110 per minute. There was a dried nasal exudate and the tonsils were enlarged and inflamed. Both lungs were clear and resonant. The heart was of normal size, the rhythm was regular, and there were no murmurs. The abdomen was flat with marked generalized voluntary rigidity. There was slight tenderness in the epigastrium with no McBurney point tenderness and an absence of the rebound phenomenon. No masses or organs were palpable. Cervical, axillary and inguinal lymphadenopathy was present but slight.

The red-cell count of the blood was 2,000,000 with 7 grams per cent of hemoglobin. The white-cell count was 33,400 with 80% polymorphonuclears, 10% band forms and 10% lymphocytes. The icterus index was 7.5 units. The sickling tests were reported negative, and the sedimentation rate of the red cells was 40 mm. per hour. Urinalysis showed a specific gravity of 1.029, an acid reaction, 20 milligrams of albumin, no sugar, one plus acetone, and a few white blood cells, finely granular and hyaline casts. The spinal fluid routine examination was negative. An x-ray of the chest showed the heart to be of normal size but of abnormal contour. A bronchitic condition in the parenchyma was suggested. A flat plate of the abdomen was interpreted as showing the liver to be somewhat enlarged.

The three day pre-operative course was as follows: The temperature range was 103° to 101° and the pulse range was 140 to 100. An enema was given on admission which produced brown liquid returns. Thereafter there were four liquid stools. During this time he vomited food or clear mucus three times. Five grains of aspirin every four hours for temperatures of 100.0° were administered on the first day. This was discontinued on the second day and sulfadiazine was substituted without clinical response being noted

on the third day. The dehydration and acidosis were easily corrected and a urinalysis on the third day showed a specific gravity of 1.016, 10 milligrams of albumin, and only a few white blood cells in the microscopic examination. Abdominal pain remained the chief complaint but it became severe, colicky and intermittent. Peristalsis was visible. The tenderness shifted to the right lower quadrant. On the third day of hospitalization an operation was performed.

Differential Diagnosis

Dr. John A. Washington: My first impression on reading this case history was that with so marked a leucocytosis, there must be a pyogenic infection localized somewhere. The longer I thought the more uncertain of this I became, because in three days there were no localizing signs. The absence of rebound tenderness in my experience speaks strongly against peritonitis or the sort of peritoneal irritation caused by appendicitis. No tenderness was described in the perirenal region. The abnormal contour of the heart suggested possibly a mediastinal abscess but the abdomen seems to have been the real center of distress. Pyelitis was pretty well ruled out.

It soon began to seem probable that the abdominal discomfort was due to some other cause. Sickle cell anemia was ruled out by blood examination; purpura, rheumatic fever and mesenteric adenitis remained as possibilities. There were no petechiae to cause one to lean toward purpura as a diagnosis. A possible clue might lie in the history of a sore knee. Although he is said to have hurt his knee, a colored boy might well be inaccurate on this point. I don't see how anyone could be sure, but with the story of the knee, I am inclined to list the probabilities as first rheumatic fever, second mesenteric adenitis, third purpura and fourth a pyogenic infection.

Please do not think that I question for a moment the advisability of exploring the patient. When in doubt, this is the only safe procedure.

Clinical Diagnosis: 1. Acute appendicitis; 2. Rheumatic fever.

Dr. Washington's Diagnosis: 1. Rheumatic fever; 2. Mesentere adenitis; 3. Purpura; 4. Pyogenic infection.

Anatomical Diagnosis: Acute rheumatic heart disease.

Pathological Discussion

Dr. Sullivan: Under ethylene and ether anesthesia an appendectomy was performed with technical ease and the appendix proved to be grossly and microscopically normal. As the incision was being closed the boy suddenly stopped breathing. It was discovered that the heart sounds were inaudible and all efforts at resuscitation were futile. Postmortem examination demonstrated an enlarged heart with marked dilatation of the right auricle

and ventricle and moderate hypertrophy of the left ventricle. The weight of the heart was 250 grams and the expected weight at nine years is about 126 grams. Along the edges of the leaflets of the mitral valve were many tiny warty vegetations which were red in color and firmly attached. The anterior cusp of the aortic valve had a small area similarly involved. The myocardium was deep red and appeared congested. Microscopically sections from the myocardium showed variations from practically normal heart muscle to areas of advanced degeneration, necrosis and inflammatory reaction. The lungs were moderately congested. The liver extended 8.5 centimeters below the costal margin and weighed twice its expected weight. Congestion was marked. The spleen was slightly enlarged and the splenic nodules were prominent. It is unlikely that there was much if any congestive heart failure before the operation and it may be that this death was due to ventricular flutter which occurs not infrequently in rheumatics.